REMARKS

Claims 78-100 are pending in the subject application. Applicants have hereinabove canceled claim 94 without disclaimer or prejudice to their right to pursue the subject matter of this claim in a later-filed application and amended claim 95. This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 78-93 and 95-100 will be pending.

Objection to the specification

The Examiner stated the prior objection to the disclosure is maintained for the reasons as set forth in the last Office Action mailed 6/10/96 (see Paper No.9). The Examiner stated that applicants submit that they will provide a new Figure 6B to overcome the rejection when the case is in condition for allowance. The Examiner stated until applicants submit a proper Figure said objection is maintained.

In response, applicants will submit a new Figure 6B upon the indication of allowable subject matter.

Obviousness-type double patenting rejection

The Examiner provisionally rejected claims 78-100 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 78-115 of copending Application No. 08/477,097 for reasons previously made of record for claims, 53, 55-57 and 59-77. The Examiner stated that applicants assert that the added new claims in the copending application obviate the obvious type double patenting. The Examiner stated Applicants'

arguments are not persuasive since the instantly claimed GM2-KLH conjugate and methods anticipate the corresponding GM2-KLH conjugate and methods of use thereof in the copending 08/477,097 application. The Examiner stated Applicants amendments are insufficient to remove the rejection.

The Examiner provisionally rejected claims 78-100 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 44 and 46-56 of copending Application Nos. 08/477, 147 for reasons previously made of record for claims 53, 55-57 and 59-77. The Examiner stated that although the conflicting claims are not identical, they are not patently distinct from each other for the reasons set forth in the prior Office Actions. The Examiner stated the instant conjugate species of GM2, GM3, GD3, GD3 lactone, o-acetyl GD3. and GT3 and methods of use thereof anticipate the conjugates and methods of the 08/477,147 application, in as much as, the '154 application claims GM2-KLH conjugates and methods of use. The Examiner stated applicants' amendments are insufficient to overcome the double patenting rejection.

The Examiner provisionally rejected claims 78-100 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the pending claims of application No 08/196,154 for reasons previously made of record for claims 53, 55-57 and 59-77. The Examiner stated that the instantly claimed composition drawn to the specific species of GM2 ganglioside conjugate to KLH, anticipates all the pending claims of 08/196,154, in as much as the '154 application claims GM2-KLH conjugates and methods of use.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants contend that the claims of the cited applications do not render obvious the claims of the subject application and therefore, an obviousness-type double patenting rejection is not appropriate. Applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 78-81 and 83-100 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the Office Action mailed October 6, 1999 (see Paper No. 20) for claims 53-57, 59-72 and new claims 73-77 and the Office Action mailed 10-5-99.

The Examiner stated as to claims 78-81 and 83-100, applicants' arguments' and amendments have been carefully considered. The Examiner stated that the claims still recite "derivatives of KLH". The Examiner stated such derivatives are not enabled for reasons already made of record. The Examiner stated that applicants' arguments and amendments are insufficient to obviate this rejection.

The Examiner stated that as to new claims 94-100, the claims are enabled for the use of the composition only for the treatment of cancer but are not enabled for the prevention of cancer, for reasons made of record in Paper No. 8, mailed June 13, 1996. The

Examiner stated that applicants' arguments have been carefully considered but are not persuasive. The Examiner stated that applicants' argue that the conjugate vaccine of the invention prevents outgrowth of micrometastases and prevents cancer per se (Zhang et al, Cancer Research 58:2844-2849, 1998). The Examiner stated this is not persuasive, the claims are not drawn to preventing outgrowth of micrometastases and the conjugate used in the paper is GD2-KLH (10 ug of GD2 conjugated to 60 ug KPH, wherein the conjugation of GD2 of KLH was achieved by conversion of the GD2 ceramide double bond to aldehyde by ozonolysis and attachment to KLH by reductive amination in the presence of cyanoborohydride) plus 10 ug QS-21. The Examiner stated thus, the conjugate of the claims is not that which has been demonstrated by the art to prevent outgrowth of micrometastases, nor does the method provide for the method of the paper (multiple doses administered by a specific route. Moreover, the article specifically teaches that the vaccine "...should be used exclusively in the adjuvant setting, where circulating tumor cells and micrometastases are the primary targets (page 2844, last line of abstract)." The Examiner stated the evidence of the paper targeted circulating cells specific type of tumor cell (lymphoma) which was administered intravenously and micrometastases thereof from circulation, which is clearly not representative of cancers or relapses as instantly claimed. The Examiner stated moreover, figure 1, demonstrates that administration of the GD2-KPH, QS-21 vaccine at days -21, -14 and -7 does not prevent cancer as demonstrated by the death of some of the experimental group after experimental intravenous challenge of lymphoma cells (see Figure 1, Experiments 3 and 6B). The Examiner stated at page 2845, column 2, second and third paragraph, Zhang et al teach that the vaccine prolonged survival, but in the discussion

of experiment 6, only 4 out of 6 vaccinated mice remained disease free at the latest time point measured. The Examiner stated moreover, Zhang et al admit that the alleged protection in Experiment 7 of Figure 1, was "not statistically significant" and moreover this experiment is not directly comparable with the other experiments because the tumor burden administered intravenously was substantially reduced. The Examiner stated clearly the vaccine when administered prior to the cancer does not prevent as claimed or as argued by applicant. The Examiner stated additionally, prevention of relapse as claimed has not been demonstrated nor specifically addressed by this paper and Zhang et al admits that "If antibodies of sufficient titer and potency to eliminate circulating cancer cells and micrometastases could be maintained in cancer patients as well, even metastic cancer would have a quite different implication. The Examiner stated with continuing showers of metastases no longer possible, aggressive treatment of primary and metastic sites might result in long term control." The Examiner stated relapsing of cancer is quite different than elimination of micrometastases (see page 2848, column 1, last paragraph) not primary cancer. The Examiner stated Zhang et al do not address primary cancer and the experimental protocols set forth therein do not address prevention of primary cancer as is claimed for prevention of relapse of cancer. The Examiner stated reduction of circulating lymphoma cells and reduction in micrometastases is not commensurate in scope with prevention of cancer or prevention of a relapse of cancer.

In response, with respect to the Examiner's above rejection concerning KLH derivatives, applicants respectfully traverse the Examiner's the rejection. Claims which recite "derivatives of KLH" are enabled. Applicants respectfully direct the Examiner's attention to page 12, lines 4-13 for examples of generating such derivatives. For example, one skilled in the art could generate a KLH derivative by directly liking it to an immunological adjuvant, such as monophospholipid A, non-ionic block copolymers or a cytokine, as taught by on page 12, lines 4-13 of the specification.

With respect to the Examiner's above rejection concerning the prevention of cancer, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claim 94 without disclaimer or prejudice to their right to pursue the subject matter of this claim in a later-filed application. In addition, applicants acknowledge the Examiner's statement that the claims are enabled for the use of the composition for the treatment. Accordingly, applicants have also hereinabove amended claim 95 such that it now recites a "method of treating a cancer in a subject." Therefore , the claimed invention is enabled.

Applicants contend that these amendments obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. 103(a)

The Examiner rejected claims 78-95 and 97-100 under 35 U.S.C. 103(a) as being unpatentable over Livingston et al. (Cancer Research) in view of Ritter et al. (Seminars in Cancer Biology),

Liane et al (Journal of Biological Chemistry), Livingston et al. (U.S. Patent No. 5,102,663), Ritter et al. (Immunobiol), Kensil et al. (The Journal of Immunology), Marciani et al. (Vaccine) and Uemura et al (J Biochem) for reasons made of record for previous claims 18-20, 53, 55-67 and 69-72 in Paper No. 23, 10-5-99.

The Examiner stated that applicants' arguments have been carefully considered but are not persuasive. The Examiner stated that applicants' contend that the references neither alone nor in combination teach the claimed invention of conjugation of the ganglioside derivative through a ceramide derived carbon. The Examiner stated this is not persuasive, the conjugation procedure as combined provides for the identical procedure as Applicants' coupling procedure. The Examiner stated moreover, the combination provides a reasonable expectation of success as demonstrated by Uemura et al which demonstrates the ozonolysis and reduction of various shingolipids did not affect the haptenic reactivity with antibodies. The Examiner stated Applicants' have neither pointed distinguishing features of applicants invention nor provided any scientific evidence or rationale which would indicate that the conjugation procedure as combined by the prior art would not arrived at the claimed product and methods. The Examiner stated Applicants arguments are not persuasive and the rejection stands across the new claims.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants contend that the cited references, namely Livingston et al. (Cancer Research) in view of Ritter et al. (Seminars in Cancer Biology), Liane et al (Journal of Biological Chemistry), Livingston et al. (U.S. Patent No. 5,102,663), Ritter et al. (Immunobiol), Kensil et al. (The Journal of Immunology), Marciani et al. (Vaccine) and Uemura et al (J Biochem) either alone or in combination do not teach, suggest or disclose applicants claimed invention and therefore do not render obvious the claimed invention and accordingly, respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. 103(a)

The Examiner rejected claim 114 under 35 U.S.C. 103(a) as being unpatentable over Livingston et al. (Cancer Research), Ritter et al. (Cancer Biology, 1991), Liane et al (Journal of Biological Chemistry), Livingston et al. (U.S. Patent No. 5,102,663), Ritter et al. (1990), Kensil et al, and Marciani et al., and Uemura et al (J Biochem) as applied to claims 69-81 and 83-96 above and further in view of Irie et al. (U.S. Patent Nol 4,557,931) for reasons made of record for claim 68 in Paper No. 23, 10-5-99. The Examiner stated that applicants' arguments have been carefully considered but are not persuasive. Applicants' contend that the references neither alone nor in combination teach the claimed invention of conjugation of the ganglioside derivative through a ceramide derived carbon. The Examiner stated that this is not persuasive, the conjugation procedure as combined provides for the identical procedure as applicants' coupling procedure. The Examiner stated moreover, the combination provides a reasonable expectation of

success as demonstrated by Uemura et al which demonstrates the ozonolysis and reduction of various sphingolipids did not affect the heptenic reactivity with antibodies. The Examiner stated Applicants' have neither pointed distinguishing features of applicants invention nor provided any scientific evidence or rationale which would indicate that the conjugation procedure as combined by the prior art would not arrived at the claimed product and methods. The Examiner stated Applicants' arguments are not persuasive and the rejection stands across the new claims.

In response, applicants respectfully traverse the Examiner's above rejection. Applicants contend that the cited references, namely Livingston et al. (Cancer Research), Ritter et al. (Cancer Biology, 1991), Liane et al (Journal of Biological Chemistry), Livingston et al. (U.S. Patent No. 5,102,663), Ritter et al. (1990), Kensil et al, and Marciani et al., and Uemura et al (J Biochem) as applied to claims 69-81 and 83-96 above and further in view of Irie et al. (U.S. Patent Nol 4,557,931) either alone or in combination do not teach, suggest or disclose applicants claimed invention and therefore do not render obvious the claimed invention and accordingly, respectfully request that the Examiner reconsider and withdraw this ground of rejection.

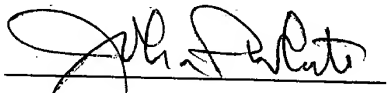
Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. claims 78-93 and 95-100.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

No fee, other than the enclosed $445.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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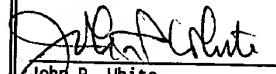
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



12/27/96
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